Claims

1. A method of directing a cellular immune response in a mammal, said method comprising administering to said mammal an effective amount of therapeutic cells, said therapeutic cells expressing a membrane-bound, proteinaceous chimeric receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is capable of signalling said therapeutic cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

2. The method of claim 1, wherein said target cell is a host cell infected with an infective agent, a tumor or cancerous cell, or an autoimmune-generated cell.

3. The method of claim 1, wherein said cellular response is MHC-independent.

4. The method of claim 1, wherein said intracellular portion is the signal-transducing portion of a T cell receptor protein, a B cell receptor protein, or an Fc receptor protein, or a functional derivative thereof.

5. The method of claim 1, wherein said chimeric receptor further comprises a transmembrane portion of said T cell receptor protein, said B cell receptor protein, or said Fc receptor protein.

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6. A method of directing a cellular immune response in a mammal, said method comprising administering to said mammal an effective amount of therapeutic cells, said therapeutic cells expressing a membrane-bound, proteinaceous chimeric receptor, said receptor comprising (a) an

extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) a transmembrane portion which is capable of signalling said therapeutic cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

7. The method of claim 6, wherein, following binding of said extracellular portion to said agent or said cell, said transmembrane portion oligomerizes with a cytolytic signal-transducing protein of said therapeutic cell resulting in destruction of said receptor-bound cell or agent.

8. The method of claim 6, wherein said transmembrane portion comprises an oligomerizing portion of a T cell receptor protein, a B cell receptor protein, or an Fc receptor protein, or a functional derivative thereof.

9. The method of claim 4, wherein said T cell receptor protein is ζ.

10. The method of claim 9, wherein said chimeric receptor comprises amino acids 421-532 of SEQ ID NO: 6, or a functional cytolytic signal-transducing derivative thereof.

11. The method of claim 9, wherein said chimeric receptor comprises amino acids (a) 423-455; (b) 438-455; (c) 461-494; or (d) 494-528 of SEQ ID NO: 6.

12. The method of claim 8, wherein said T cell receptor protein is ζ.

13. The method of claim 12, wherein said chimeric receptor comprises amino acids 400-420 of SEQ ID NO: 6.

14. The method of claim 4, wherein said T cell receptor protein is η.

15. The method of claim 14, wherein said chimeric receptor comprises amino acids 421-575 of SEQ ID NO: 4, or a functional cytolytic signal-transducing derivative thereof.

16. The method of claim 14, wherein said chimeric receptor comprises amino acids (a) 423-455; (b) 438-455; (c) 461-494; or (d) 494-528 of SEQ ID NO: 4.

17. The method of claim 8, wherein said T cell receptor protein is η.

18. The method of claim 17, wherein said chimeric receptor comprises amino acids 400-420 of SEQ ID NO: 4.

19. The method of claim 4, wherein said Fc receptor protein is γ.

20. The method of claim 19, wherein said chimeric receptor comprises amino acids 421-462 of SEQ ID NO:5, or a functional cytolytic signal-transducing derivative thereof.

21. The method of claim 8, wherein said Fc receptor protein is γ.

22. The method of claim 21, wherein said chimeric receptor comprises amino acids 402-419 of SEQ ID NO:5.

23. The method of claim 21, wherein said chimeric receptor comprises amino acids Tyr282-Tyr298 inclusive of Fig. 15A.

24. The method of claims 4 or 8, wherein said Fc receptor protein is human FcγRIII, human FcRIIγA, or human FcRIIγC.

25. The method of claims 4 or 8, wherein said T cell receptor protein is CD3 delta.

26. The method of claim 25, wherein said chimeric receptor protein comprises amino acids 132-171 of Fig. 16 (SEQ ID NO: 24).

27. The method of claims 4 or 8, wherein said T cell receptor protein is T3 gamma.

28. The method of claim 27, wherein said chimeric receptor protein comprises amino acids 140-182 of Fig. 17 (SEQ ID NO: 25).

29. The method of claims 4 or 8, wherein said B cell receptor protein is mb1.

30. The method of claim 29, wherein said chimeric receptor protein comprises amino acids 162-220 of Fig. 18 (SEQ ID NO: 26).

31. The method of claims 4 or 8, wherein said B cell receptor protein is B29.

32. The method of claim 31, wherein said chimeric receptor protein comprises amino acids 183-228 of Fig. 19 (SEQ ID NO: 27).

33. The method of claims 1 or 6, wherein said therapeutic cells are selected from the group consisting of:

(a) T lymphocytes;

(b) cytotoxic T lymphocytes:
(c) natural killer cells;
(d) neutrophils;
(e) granulocytes;
(f) macrophages;
(g) mast cells;
(h) HeLa cells; and
(i) embryonic stem cells (ES).

34. The method of claims 1 or 6, wherein said target infective agent is an immunodeficiency virus.

35. The method of claims 1 or 6, wherein said extracellular portion comprises an HIV envelope-binding portion of CD4, or a functional HIV envelope-binding derivative thereof.

36. The method of claims 1 or 6, wherein said HIV-envelope binding portion of CD4 comprises the peptide encoded by nucleotides 1-369 of SEQ ID NO:1.

37. The method of claims 1 or 6, wherein said therapeutic cells further express a membrane-bound, proteinaceous chimeric receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is derived from CD28.

38. The method of claims 1 or 6, wherein said therapeutic cells destroy said receptor-bound target cell or target infective agent by cytolysis.

39. A cell which expresses a proteinaceous membrane-bound chimeric receptor, said receptor comprising

(a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) an intracellular portion derived from a T cell receptor, a B cell receptor, or an Fc receptor which is capable of signalling said cell to destroy a receptor-bound target cell or receptor-bound target infective agent.

40. The cell of claim 39, wherein said target cell is a host cell infected with an infective agent, a tumor or cancerous cell, or an autoimmune-generated cell.

41. The cell of claim 39, wherein said binding is MHC-independent.

42. The cell of claim 39, wherein said intracellular portion is the signal-transducing portion of a T cell receptor protein, a B cell receptor protein, or an Fc receptor protein, or a functional derivative thereof.

43. The cell of claim 42, wherein said chimeric receptor further comprises a transmembrane portion of said T cell receptor protein, said B cell receptor protein, or said Fc receptor protein.

44. A cell expressing a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc receptor which is capable of signalling said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

45. The cell of claim 44, wherein, following binding of said extracellular portion to said cell or agent, said transmembrane portion oligomerizes with a cytolytic signal-transducing protein of said receptor-bearing cell resulting in destruction of said receptor-bound agent or cell.

46. The cell of claim 44, wherein said binding is MHC-independent.

47. The cell of claims 44, wherein said transmembrane portion comprises an oligomerizing portion of a T cell receptor protein, a B cell receptor protein, or an Fc receptor protein, or a functional derivative thereof.

48. The cell of claim 42, wherein said T cell receptor protein is ζ.

49. The cell of claim 48, wherein said chimeric receptor comprises amino acids 421-532 of SEQ ID NO: 6, or a functional cytolytic signal-transducing derivative thereof.

50. The cell of claim 48, wherein said chimeric receptor comprises amino acids (a) 423-455; (b) 438-455; (c) 461-494; or (d) 494-528 of SEQ ID NO. 6.

51. The cell of claim 47, wherein said T cell receptor protein is ζ.

52. The cell of claim 51, wherein said chimeric receptor comprises amino acids 400-420 of SEQ ID NO: 6.

53. The cell of claim 42, wherein said T cell receptor protein is η.

54. The cell of claim 53, wherein said chimeric receptor comprises amino acids 421-575 of SEQ ID NO: 4, or a functional cytolytic signal-transducing derivative thereof.

55. The cell of claim 53, wherein said chimeric receptor comprises amino acids (a) 423-455; (b) 438-455; (c) 461-494; or (d) 494-528 of SEQ ID NO: 4.

56. The cell of claim 47, wherein said T cell receptor protein is η.

57. The cell of claim 56, wherein said chimeric receptor comprises amino acids 400-420 of SEQ ID NO: 4.

58. The cell of claim 42, wherein said Fc receptor protein is γ.

59. The cell of claim 58, wherein said chimeric receptor comprises amino acids 421-462 of SEQ ID NO:5, or a functional cytolytic signal-transducing derivative thereof.

60. The cell of claim 47, wherein said Fc receptor protein is γ.

61. The cell of claim 60, wherein said chimeric receptor comprises amino acids 402-419 of SEQ ID NO: 5.

62. The cell of claim 60, wherein said chimeric receptor comprises amino acids Tyr282-Tyr298 inclusive of Fig. 15A.

63. The cell of claims 42 or 47, wherein said Fc receptor protein is human FcγRIII, human FcRIIγA, or human FcRIIγC.

64. The cell of claims 42 or 47, wherein said T cell receptor protein is CD3 delta.

65. The cell of claim 64, wherein said chimeric receptor protein comprises amino acids 132-171 of Fig. 16 (SEQ ID NO: 24).

66. The cell of claims 42 or 47, wherein said T cell receptor protein is T3 gamma.

67. The cell of claim 66, wherein said chimeric receptor protein comprises amino acids 140-182 of Fig. 17 (SEQ ID NO: 25).

68. The cell of claims 42 or 47, wherein said B cell receptor protein is mb1.

69. The cell of claim 68, wherein said chimeric receptor protein comprises amino acids 162-220 of Fig. 18 (SEQ ID NO: 26).

70. The cell of claims 42 or 47, wherein said B cell receptor protein is B29.

71. The cell of claim 70, wherein said chimeric receptor protein comprises amino acids 183-228 of Fig. 19 (SEQ ID NO: 27).

72. The cell of claims 39 or 44, wherein said extracellular portion comprises the ligand-binding portion of a receptor, the receptor-binding portion of a ligand, the antigen-binding portion of an antibody, or a functional derivative thereof.

73. The cell of claims 39 or 44, wherein said target infective agent is an immunodeficiency virus or said target cell is a host cell infected with an immunodeficiency virus.

74. The cell of claim 73, wherein said extracellular portion comprises an HIV envelope-binding portion of CD4, or a functional derivative thereof.

75. The cell of claim 73, wherein said HIV-envelope binding portion of CD4 comprises the peptide encoded by nucleotides 1-369 of SEQ ID NO:1.

76. The cell of claims 39 or 44, wherein said cell further expresses a membrane-bound, proteinaceous chimeric receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding said target cell or said target infective agent, and (b) an intracellular portion which is derived from CD28.

77. The cell of claims 39 or 44, wherein said cell destroys said receptor-bound target cell or target infective agent by cytolysis.

78. A cell which expresses a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) an intracellular portion derived from a T cell receptor CD3, zeta, or eta polypeptide, a B cell receptor, or an Fc receptor.

79. A cell which expresses a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a

target infective agent, and (b) a transmembrane portion derived from a T cell receptor CD3, zeta, or eta polypeptide, a B cell receptor, or an Fc receptor.

80. The cell of claims 78 or 79, wherein said chimeric receptor includes a CD16 or CD5 extracellular portion.

81. The cell of claims 78 or 79, wherein said chimeric receptor includes a CD5 or CD7 transmembrane portion.

82. The cell of claims 78 or 79, wherein said chimeric receptor includes a CD5 or CD7 intracellular portion.

83. DNA encoding a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) an intracellular portion derived from a T cell receptor, a B cell receptor, or an Fc receptor which is capable of signalling said cell to destroy a receptor-bound target cell or receptor-bound target infective agent.

84. DNA encoding a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor, a B cell receptor, or an Fc receptor which is capable of signalling said cell to destroy a receptor-bound target cell or a receptor-bound target infective agent.

85. DNA encoding a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) an intracellular portion derived from a T cell receptor CD3, zeta, or eta polypeptide, a B cell receptor, or an Fc receptor.

86. DNA encoding a proteinaceous membrane-bound chimeric receptor, said receptor comprising (a) an extracellular portion which is capable of specifically recognizing and binding a target cell or a target infective agent, and (b) a transmembrane portion derived from a T cell receptor CD3, zeta, or eta polypeptide, a B cell receptor, or an Fc receptor.

87. DNA having a sequence substantially similar to the sequence shown in SEQ ID NO:1.

88. DNA having a sequence substantially similar to the sequence shown in SEQ ID NO:2.

89. DNA having a sequence substantially similar to the sequence shown in SEQ ID NO:3.

90. A vector comprising the chimeric receptor DNA of any of claims 83-86.

91. An antibody which specifically recognizes and binds a chimeric receptor of claims 39 or 44.

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